REMARKS

Reconsideration and allowance of pending claims 1 and 3-24 is respectfully requested. Claim 2 has been canceled and the subject matter thereof incorporated into amended claim 1. Claims 1, and 5-24 have been amended to correct informalities. The parentheticals have been removed and the European use of a comma as a decimal point has been amended to conform with U.S. patent practice. Claims 3-4 have been amended to correct for lack of antecedence. Claim 22 has been amended to delete the phrase beginning with "for example...". Support for these amendments to the claims can be found throughout the application as filed. Applicants respectfully submit that no new matter will be introduced into the application as filed via the amended claims.

Claims 1-24 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Engel et al., and Albano et al., and Felberbaum et al., and Garfield in view of Deghenghi and Rabasseda and Kent. The Examiner argues that Engel teaches a method of using an LHRH-antagonist for suppressing premature ovulation in controlled ovarian stimulation and assisted reproductive techniques. Albano is cited for its teaching of a method of using cetrorelix in suppression of premature ovulation in controlled ovarian stimulation and assisted reproductive techniques, such as IVF and ICSI. Albano is also noted by the Examiner for its teaching that progesterone concentration is significantly lowered due to the administration of cetrorelix. The Examiner cites Felberbaum for its teaching of the usefulness of LHRH-antagonists in a method of suppression of premature ovulation in controlled ovarian and assisted reproductive techniques. Felberbaum is also noted for teaching a fall of sex steroids due to the administration of LHRH-

antagonists. Garfield is cited by the Examiner for its disclosure of the use of progestogen, together with an estrogen and an LHRH-antagonist, during follicular phase in a method of controlling ovarian stimulation and preventing conception. Deghnghi is cited for its teaching of the LHRH-antagonists cetrorelix, teverelix, ganirelix and antide. Rabasseda is cited for teaching that LHRH-antagonists such as cetrorelix, ganirelix, and abarelix are known in the treatment of female infertility. The Examiner notes Kent discloses that the combination of progestogens and estrogen is useful in animal contraception.

The Examiner asserts that it would have been obvious to a skilled artisan at the time the invention was made to "employ the particular LHRH-antagonist such as teverelix, antide, and abarelix and to optimize their effective amounts to be administered, and to schedule or program the ovarian stimulation therapy on Fridays to Mondays and oocyte pick up and ART on Mondays to Thursdays, to employ the particular estrogen, mestranol, in oral contraceptive preparations along with progestogen". *See* outstanding Office Action at page 7. Applicants traverse for at least the following reasons.

The cited combination of art fails to disclose the program and the novel combination of steps that comprises the claimed invention. The inventive method provides for the first time the use of an LHRH-antagonist in controlled ovarian stimulation cycles programmed by oral contraceptives. *See* instant specification at page 5, lines 23-29. The Example shows that the inventive protocol produces similar clinical responses as are observed in non-programmed cycles. The Examiner admits that the cited art fails to disclose the claimed program of ovarian stimulation by the administration of oral contraceptive preparations or the effective

amounts of the LHRH-antagonists to be administered during the method. *See* outstanding Office Action at page 6. Therefore, the claims are neither suggested nor rendered obvious by the cited art. Applicants respectfully submit that the Section 103-based rejection should be withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully submit that the application is in condition for allowance. Notification to that effect is earnestly solicited. Should questions relating to patentability remain, the Examiner is invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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APPENDIX

MARK UP VERSION SHOWING CHANGES MADE

IN THE CLAIMS:

The claims have been amended as indicated below.

1. (Twice Amended) In the method of therapeutic management of infertility by programming of controlled ovarian stimulation [(COS)] and assisted reproductive procedures [(ART)] the improvement consisting of :

a) suppression of premature ovulation with an LHRH-antagonist in controlled ovarian stimulation [(COS)] and assisted reproductive techniques [(ART)] with multiple follicle and oocyte development;

b) programming the start of controlled ovarian stimulation [(COS)] by the administration to a patient of progestogen [-] only -preparations or , alternatively, combined oral contraceptive preparations;

c) exogenous stimulation of the ovarian follicle growth;

d) ovulation induction with HCG, native LHRH, LHRH-agonists or recombinant LH; and

e) application of assisted reproduction techniques, especially of IVF, ICSI, GIFT, ZIFT or by intrauterine insemination by sperm injection,

wherein onset of the patient's menstrual cycle and of controlled ovarian stimulation are programmed in order to perform oocyte pickup and fertilization procedures during Mondays to Fridays.

3. (Amended) The method of claim 1 wherein the programming of the [start] onset of the menstrual cycle and of controlled ovarian stimulation procedures oral

contraceptives or progestogen-only containing preparations are given in the follicular phase [, preferably] starting at menstrual cycle day 1 or 2 or in the late luteal phase of the previous menstrual cycle.

4. (Amended) The method of claim 1 wherein the intake of the [last tablet] progestogen only -preparations or combined oral contraceptive preparations is completed on [will preferably be on a] Mondays to Thursdays to obtain start of menstrual bleeding and of ovarian stimulation therapy on Fridays to Mondays and, thereafter, oocyte pick up and further ART procedures can be scheduled and undertaken on Mondays to Thursdays.

5. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the LHRH-antagonist is cetrorelix.

6. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the LHRH-antagonist is teverelix.

7. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the LHRH-antagonist is ganirelix.

8. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the LHRH-antagonist is antide.

9. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the LHRH-antagonist is abarelix.

10. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the programming is performed by oral administration of progestogen preparations.

11. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the programming is performed by oral administration of progestogen-only containing contraceptives.

12. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the programming is achieved by oral administration of combined monophasic contraceptive preparations containing ethinylestradiol and progestogen.

13. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the programming is undertaken by oral administration of biphasic contraceptive preparations containing ethinylestradiol and progestogen.

14. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the programming is performed by oral administration of triphasic contraceptive preparations containing ethinylestradiol and progestogen.

15. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the programming is performed by oral administration of contraceptive preparations containing mestranol and progestogen.

16. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the programming is performed by the LHRH antagonist cetrorelix with a dosage of [0,5] 0.5 to 10 mg administered during luteal phase.

17. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique

procedures according to claim 1 in which the programming is performed by the LHRH antagonist teverelix with a dosage of [0,5] 0.5 to 10 mg administered during luteal phase.

18. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the programming is performed by the LHRH antagonist ganirelix with a dosage of [0,5] 0.5 to 10 mg administered during luteal phase.

19. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the programming is performed by the LHRH antagonist antide with a dosage of [0,5] 0.5 to 10 mg administered during luteal phase.

20. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the programming is performed by the LHRH antagonist abarelix with a dosage of [0,5] 0.5 to 10 mg administered during luteal phase.

21. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the stimulation is performed by

administration of urinary or recombinant FSH or HMG, with or without recombinant LH.

22. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the ovarian stimulation is achieved with [antioestrogens as for example] clomiphene.

23. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the ovarian stimulation is achieved with the combination of antioestrogens with gonadotropins.

24. The method of therapeutic management of infertility by programming of [COS] controlled ovarian stimulation and [ART] assisted reproductive technique procedures according to claim 1 in which the ovarian stimulation is achieved with the combination of clomiphene with gonadotropins.

ABSTRACT

A method of therapeutic management of infertility by programming of controlled ovarian stimulation and assisted reproductive procedures is disclosed containing the steps of a) suppression of premature ovulation with an LHRH-antagonist in controlled ovarian stimulation and assisted reproductive techniques with multiple follicle and oocyte development; b) programming the start of controlled ovarian stimulation by the administration to a patient of progestogen only - preparations or, alternatively, combined oral contraceptive preparations; c) exogenous stimulation of the ovarian follicle growth; d) ovulation induction with HCG, native LHRH, LHRH-agonists or recombinant LH; and e) application of assisted reproduction techniques, especially of IVF, ICSI, GIFT, ZIFT or by intrauterine insemination by sperm injection, wherein onset of the patient's menstrual cycle and of controlled ovarian stimulation are programmed in order to perform oocyte pickup and fertilization procedures during Mondays to Fridays.